REMARKS

Status of the Application

Claims 1 and 4 are pending in the present application.

In order to further business interests and without acquiescing to any of the arguments raised by the Examiner while expressly reserving the right to prosecute the same claims as originally filed (or claims similar thereto) in subsequent application(s); the Applicants have amended claims 1 and 4. Specifically, claims 1 and 4 have been amended by adding the element of "chain" to clause "a) ii)" in each claim. Support for this amendment is provided by the chemical structures of the "bifunctional linker arm" illustrated in Table 1, 2, and 3, on page 16-17, 18 and 19, and Figures 1A, 1B, 2A, 2B, 3, 4, and 5 in the application as filed. These amendments introduce no new matter.

Claims 1 and 4 have been rejected on the following grounds:

1. Claims 1 and 4 stand rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the written description requirement.
2. Claims 1 and 4 stand rejected under 35 U.S.C. §102(e) as being anticipated by U.S. patent 6,255,476 to Vinayak *et al.*

The Applicants believe the present amendments and the following remarks traverse the Examiner's rejection of the claims. These remarks are presented in the same order as they appear above.

1. The Claims Satisfy 35 U.S.C. §112, First Paragraph

The Examiner rejects Claims 1 and 4 under 35 U.S.C. §112, first paragraph, as failing to comply with the written description requirement. In order to comply with this requirement, the specification need show how "as of the filing date sought, [that the inventor] was in possession of the invention." See, *Vas Cath* v. *Mahurkar.*[1] To meet this standard, the Applicants may demonstrate their "possession" of the claimed invention by using "descriptive means as words,

[1] 935 F.2d 1555, 1560 19 USPQ2d 1111, 1117 (Fed. Cir. 1991).

structures, figures, diagrams, formulas, etc., that fully set forth the claimed invention." See, *Lockwood* v. *American Airlines Inc.*[2].

Furthermore, as the Examiner correctly notes, "[i]n analyzing whether the written description requirement is met, it is first determined whether a representative number of species have been described by their complete structure. Next, it is determined whether a representative number of species have been sufficiently described by other relevant identifying Characteristics."[3] The Examiner alleges that:

> "The claims recite a bifunctional linker arm comprising a hydrocarbon, a protected secondary amine, and a hydroxyl group. The claimed genus potentially encompasses a large number of chemical compounds that comprises a secondary amine and a hydroxyl group since hydrocarbon can be any structure which comprises carbon and hydrogen. In view of this huge genus as claimed, the compounds listed in Table 1, 2 and 3 do not constitutes a representative number of species for this vast genus. The specification also fails to describe the essential structure of said bifunctional linker that is responsible for their function as a bifunctional linker." [4]

The Examiner need only turn to the Applicants' specification to find detailed teachings which rebut this very same argument. Specifically, the Applicants state that:

> "As used herein, the term "bifunctional linker" and "bifunctional linker arm" refer to a compound that ***can link two additional compounds together by chemically interacting with both of them simultaneously***. In the present invention, one example of a suitable linker is a phosphoramidite. In the present invention, for example, a bifunctional linker arm is where one functional group is suitable for coupling with the 5' hydroxyl group of an oligonucleotide and the second functional group is suitable for coupling with an available functionality on the label compound." [5] (Emphasis added)

More specifically, in the General Description section, the Applicants teach that:

> "Following the activation of the carboxyl functional group, the tetramethylrhodamine is reacted with a bifunctional linker arm . . . . Such a linker arm serves several functions. It ***provides needed distance between the label and the oligonucleotide***, a functional group, in this case an amine; appropriate for reaction with the tetramethylrhodamine and a functional group, in this case a hydroxyl, which will ultimately allow for the coupling to the 5' hydroxyl of a support-bound protected oligonucleotide." [6] (Emphasis added)

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2 107 F.3d 1565, 1572,41 USPQ2d 1961, 1966 (Fed. Cir. 1997).
3 Office Action Mailed November 15, 2004, p. 3, ¶ 2.
4 Office Action Mailed November 15, 2004, p. 3, ¶ 2.
5 Page 8, ll. 5-11, ¶ 32 of the application filed on June 28, 2001.
6 Page 11, ll. 15-24, ¶ 51 of the application filed on June 28, 2001.

Therefore, the Applicants have, with particularity, fully "describe the essential structure of said bifunctional linker that is responsible for their function as a bifunctional linker" as requested by the Examiner in the pending Office Action.

Furthermore, in order to advance business interests and without acquiescing to the Examiner's arguments (while expressly reserving the right to prosecute the claims as filed or claims similar thereto), the Applicants have amended the pending claims to recite a "hydrocarbon chain" in place of "hydrocarbon." This claim element is supported in the application as filed. Specifically, the chemical structures of the "bifunctional linker arm", provided in Table 1, 2, and 3 and Figures 1A, 1B, 2A, 2B, 3, 4, and 5 of the application as filed, provide a representative number of species having a "hydrocarbon chain." The Examiner is reminded the drawings alone may provide a "written description" of an invention as required by § 112. See, *Vas-Cath, Inc. v. Mahurkar, 19 USPQ 2d 1111, 1118 (Fed. Cir. 1991).* Therefore, it is permissible to use the Drawings as support for this claim element.

Moreover, the Applicants have described (in Tables 1, 2, and 3) "a representative number of species" of bifunctional linker arms "by their complete structure." The Applicants submit the combination of the expository sections, from the specification as referenced above, with the chemical structures set out in Tables 1, 2, and 3; provide a teaching sufficient to enable the scope of the pending claims. The Applicants, therefore, respectfully request the Examiner withdraw the rejection raised under 35 U.S.C. § 112.

2. The Claims Are Not Anticipated Under 35 U.S.C. § 102(e)

A. Prosecution History

The art relied on by the Examiner in the instant Office Action was previously cited[7] and subsequently rebutted,[8] by the Applicants, during the protracted prosecution of this case. That is to say, after rebutting U.S. patent 6,255,476 to Vinayak, in a prior Response, the Examiner withdrew the rejection under 35 U.S.C. § 102(e) in view of the '476 patent.[9] Indeed, the procedural posture of the case strongly suggests the Applicants have successfully rebutted the art

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7 The Examiner raised the same objection, in view of the '476 patent to Vinayak, in the Office Action mailed on September 30, 2002.

8 The Applicants traversed the objection in Response to said Office Action mailed on March 31, 2003.

9 The Examiner withdrew the objection, in view of 35 U.S.C. § 102(e), in the Office Action mailed on June 17, 2003.

cited to date. Inexplicably, however, the Examiner drags out art that has already been successfully traversed to resurrect a rejection under 35 U.S.C. § 102(e). The Examiner is reminded the MPEP admonishes that the, "shortest path to the final disposition of an application is. . . finding the best references on the first search and carefully applying them."[10] Similarly, Examiners are advised that, "[p]iecemeal examination should be avoided as much as possible" and that an Examiner should avoid, "undue multiplication of references."[11] However, it is plain (even from a cursory review of the file history) the Examiner has completely ignored these maxims during the prosecution of this case. Based on these observations of the prosecution history alone, therefore, the Applicants submit the Examiner need withdraw the pending rejection under 35 U.S.C. 102(e).

B. The Invention as Amended is Not Anticipated by U.S. Patent No. 6,565,764 to Vinayak *et al.*

The Examiner states that,

> "Vinayak *et al.* teach a method of labeling an oligonucleotide bound at its 3' end to a polystyrene support by reacting the oligonucleotide with an amino-linker phosphoramidite reagent (See Figure 2, especially structure 1 in Figure 2, which is a bifunctional linker comprising hydrocarbon, protected secondary amine and hydroxyl group, and Figure). The protected amino group is detritylated (thus deprotected) then reacted with an activated label, such as TAMRA-CO_2H. Other labels taught for use in the method include: 6-FAM, rhodamines (see col. 14, 1st structure) and fluoresceins (see col.13-17). Therefore, Vinayak *et al.* disclose the instantly claimed inventions." [12]

The TAMRA label (and indeed all other labels disclosed in the '476 patent to Vinayak *et al.*), are silent on an *unactivated* label which is subsequently reacted, *in situ*, to form an *activated* label. For example, Vinayak *et al.* describe (in Figure 2) an,

> "[E]xemplary route to a labelled-support (ii) where the linker 1 (X-Y- P_1) is converted to 2 (A-X-Y-P_1) and attached to aminomethyl, highly-cross linked polystyrene 3. The resulting product 4 is deprotected to 5. ***A pre-activated label, e.g. TAMRA-NHS*** (N-hydroxysuccinimide ester of 5-carboxy tetramethylrhodamine) is covalently attached to 5 to yield the labelled-support 6, ready for oligonucleotide synthesis."[13] (Emphasis added)

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10 MPEP § 707.02

11 MPEP § 707.07(g)

12 Office Action Mailed November 15, 2004, p. 4, ¶ 4.

13 U.S. Patent 6,255,476 to Vinayak *et al.*, col. 9, lines 19-26.

In contrast, the currently claimed embodiments of the present invention describe the *in situ* conversion of an unactivated label to an activated label. In particular, this *in situ* conversion is highlighted in Figure 3 which describes an "In Situ-Produced Activated TMR" in the projected reactions.[14] Given that Vinayak is silent on a method wherein an unactivated label is reacted, *in situ*, to form an activated label which is further reacted with a support bound linker-oligonucleotide, thereby, producing a labeled support-bound protected oligonucleotide, the reference does not teach each and every element of the claimed embodiment of the present invention and, therefore, cannot anticipate these same claims. Once again, therefore, the Applicants respectfully request the pending rejections, under 35 U.S.C. §102(e), be withdrawn.

CONCLUSION

For the reasons set forth above, it is respectfully submitted that Applicants' claims as amended should be passed to allowance. Should the Examiner believe that a telephone interview would aid in the prosecution of this application, the Applicants encourages the Examiner to call the undersigned collect at (617) 252-3353.

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[14] See (in part), page 12, lines 25-29 and page 13, lines 1-3 of the application as filed.